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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 17:53:37 ON 08 MAY 2006

=> file medline, biosis, embase, dgene, wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.05	1.05

FILE 'MEDLINE' ENTERED AT 17:56:19 ON 08 MAY 2006

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=> s factor VIII:C
L1 2001 FACTOR VIII:C

=> s l1 and salt
L2 16 L1 AND SALT

=> s l1 and cation exchange
L3 1 L1 AND CATION EXCHANGE

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 1 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Preparation of factor VIII-von Willebrandt factor complexes.
AN 2000-170748 [15] WPIDS
CR 1998-481146 [41]
AB WO 9943712 A UPAB: 20060505

NOVELTY - Preparation of a **factor VIII:C**/vWF complex from plasma or a plasma fraction uses ion exchange chromatography. The obtained complex has 300-fold purity and the yield is at least 50% of the **factor VIII:C** and vWF compared to cryoprecipitate or analogue plasma fractions.

USE - No further details.

Dwg.0/0

ACCESSION NUMBER: 2000-170748 [15] WPIDS
CROSS REFERENCE: 1998-481146 [41]
DOC. NO. CPI: C2000-052978
TITLE: Preparation of factor VIII-von Willebrandt factor complexes.
DERWENT CLASS: B04
INVENTOR(S): LINNAU, Y; SCHOENHOFER, W
PATENT ASSIGNEE(S): (BAXT) BAXTER AG; (IMMO) IMMUNO AG
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9943712	A1	19990902	(200015)*	GE	15
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9925030	A	19990915	(200015)		
EP 1056779	A1	20001206	(200064)	GE	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
AT 9800866	A	20010415	(200130)		
AT 408443	B	20011015	(200170)		
JP 2002504561	W	20020212	(200215)		12
US 6605222	B1	20030812	(200355)		
EP 1056779	B1	20060426	(200629)	GE	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9943712	A1	WO 1999-AT48	19990225
AU 9925030	A	AU 1999-25030	19990225
EP 1056779	A1	EP 1999-904614	19990225
		WO 1999-AT48	19990225
AT 9800866	A	AT 1998-866	19980520
AT 408443	B	AT 1998-866	19980520
JP 2002504561	W	WO 1999-AT48	19990225
		JP 2000-533462	19990225
US 6605222	B1	WO 1999-AT48	19990225
		US 2001-623245	20010319
EP 1056779	B1	EP 1999-904614	19990225
		WO 1999-AT48	19990225

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9925030	A	Based on	WO 9943712
EP 1056779	A1	Based on	WO 9943712
AT 408443	B	Previous Publ.	AT 9800866
JP 2002504561	W	Based on	WO 9943712
US 6605222	B1	Based on	WO 9943712

EP 1056779 B1 Based on WO 9943712

PRIORITY APPLN. INFO: AT 1998-866 19980520; WO 1998-AT43 19980227

=> d l2 ti abs ibib tot

L2 ANSWER 1 OF 16 MEDLINE on STN

TI **Factor VIII:c** concentrate virus inactivated: progress in purification by using classic chromatographic methods.

AB This study was carried out with the aim of developing a production process for the manufacture of a highly purified factor VIII concentrate which is virus inactivated by pasteurization in liquid phase. Beside standard plasma protein separation techniques, the procedure uses a chromatographic step on anion exchanger, whose selectivity is increased by using high, but not destabilizing **salt** concentrations. The final product before stabilization has a specific activity higher than 300 IU/mg of protein, namely the highest specific activity reported for human factor VIII concentrates purified without the use of immunoadsorbents.

Does not use Cation exchange

ACCESSION NUMBER: 93190537 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8447116
TITLE: **Factor VIII:c** concentrate virus inactivated: progress in purification by using classic chromatographic methods.
AUTHOR: Arrighi S; Pacenti L; Borri M G
CORPORATE SOURCE: Sclavo Biotechnology Center, Siena, Italy.
SOURCE: Vox sanguinis, (1993) Vol. 64, No. 1, pp. 13-8.
Journal code: 0413606. ISSN: 0042-9007.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 16 Apr 1993
Last Updated on STN: 16 Apr 1993
Entered Medline: 5 Apr 1993

L2 ANSWER 2 OF 16 MEDLINE on STN

TI The assay of **factor VIII: C** in heparinized plasma: a polybrene neutralization method.

AB Factor VIII coagulant activity (VIII:C) has been shown by several investigators to exhibit increased stability in vitro when physiological levels of plasma ionized calcium are maintained by anticoagulation with heparin rather than citrate. An increase in initial activity of VIII:C in heparin over that of VIII:C in citrate has been reported but this has not been confirmed. In order to assay VIII:C in heparinized plasma, the heparin anticoagulant effect must be excluded without interfering with the validity of the assay. A one-stage clotting assay for VIII:C has been developed where heparin is neutralized by Polybrene, a synthetic polymerized quaternary ammonium **salt**. VIII:C may be accurately measured by this method which satisfies the requirements for a valid assay of parallelism and linearity.

ACCESSION NUMBER: 86208962 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3085265
TITLE: The assay of **factor VIII: C** in heparinized plasma: a polybrene neutralization method.
AUTHOR: Cumming A M; Wensley R T; Delamore I W
SOURCE: Thrombosis and haemostasis, (1986 Feb 28) Vol. 55, No. 1, pp. 58-60.
Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198605
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 30 May 1986

L2 ANSWER 3 OF 16 MEDLINE on STN
TI Isolation of human **factor VIII:C** by preparative high-performance size-exclusion chromatography.
AB Human Factor VIII procoagulant protein (VIII:C) is a plasma protein that participates in the cascade of events leading to blood coagulation. It is absent or defective in patients with hemophilia A. In vivo **Factor VIII:C** associates with Von Willibrand factor and its multimers to form a high-molecular-weight particle that can be dissociated into a lower-molecular-weight form in the presence of high concentrations of **salt**. We have been able to purify rapidly **Factor VIII:C** on a large scale by sequential high-performance size-exclusion chromatography (HPSEC) under conditions of first low **salt** and then high **salt** concentration. Reconstituted commercial **Factor VIII:C** concentrate was purified by chromatography on a preparative HPSEC column (Toyo Soda, 60 X 2.5 cm, 300 ml) in 0.05 M imidazole buffer, (pH 7.0), containing 0.15 M sodium chloride. **Factor VIII:C** activity was eluted in the void volume in less than 20 min as a high-molecular-weight particle, well separated from low-molecular-weight contaminants. Purification was 20-fold, with a yield of 80%. Up to 4 g of Factor VIII concentrate could be purified at one time in this manner. This material was then concentrated and made 0.35 M in calcium chloride prior to re-chromatography on the same column in a buffer containing 0.30 M calcium chloride. Under these conditions, **Factor VIII:C** activity was eluted in the inner volume of the column at a position corresponding to a molecular weight of several hundred thousand in less than 1 h. It was well separated from both larger proteins and smaller peptide fragments. (ABSTRACT TRUNCATED AT 250 WORDS)
ACCESSION NUMBER: 85289636 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3928665
TITLE: Isolation of human **factor VIII:C** by preparative high-performance size-exclusion chromatography.
AUTHOR: Herring S W; Shitanishi K T; Moody K E; Enns R K
SOURCE: Journal of chromatography, (1985 Jun 19) Vol. 326, pp. 217-24.
Journal code: 0427043. ISSN: 0021-9673.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 11 Oct 1985

L2 ANSWER 4 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI Four hydrophobic amino acids of the factor VIII C2 domain contribute to the membrane-binding motif.
AB Factor VIII (fVIII) binds to phospholipid (PL) membranes via a motif localized to the C2 domain. The recently published crystal structure of the C2 domain has prompted a model in which membrane binding is mediated by hydrophobic residues on one end of the beta-barrel, a net charge provided by a ring of positively charged residues, and by specific hydrogen bonds and a **salt** bridge to a phospho-L-serine motif. To probe this model we have prepared 13 fVIII mutants in which amino

acid(s) were changed to alanine by site-directed mutagenesis. Mutations were screened by transient expression in COS cells. Harvested media was analyzed using a one-stage aPTT, ELISA, metabolic labeling, and in a Xase assay altered to have limiting PL. Positive charge mutants R2215, R2220, K2249, and K2227 and neutral mutants Q2213, N2217, W2313, and F/T 2196/2197 were secreted and had specific activities within 30% of wild-type fVIII. Mutants of R2209 and R2320 were not secreted and metabolic labelling indicated intracellular degradation. Hydrophobic mutants M/F 2199/2200 and L/L 2251/2252 led to 33% and 41% reduction, respectively, in specific activity in the APTT assay but normal activity in the Coamatic assay which has a higher PL content. In the PL-limiting factor Xase assay (sonicated vesicles of PS:PE:PC 4:20:76, 0.15 muM PL) the mutants had 89 +- 6% and 72 +- 11% reduction, respectively, in specific activity. To confirm that these mutants have defective PL binding they were prepared on a larger scale and the conditioned media was concentrated by ultrafiltration, separated from vWf with 0.35 M CaCl2, and loaded onto micro-columns (10 mul bed volume) of anti fVIII-Superose. The Superose-bound fVIII was removed from micro-columns and binding of fluorescent PL vesicles (sonicated vesicles of PS:PE:PC:NBD-PC 4:20:75:1) to immobilized fVIII was measured by flow cytometry. Vesicle-binding capacity was normalized to the quantity of fluorescein-labeled Delta-Pro vWf which bound to the same immobilized fVIII mutants at a Delta-Pro vWf concentration of 82 nM. The results indicated a reduction in PL vesicle affinity of > 90% for both mutants. Our results indicate that the two hydrophobic motifs composed of M/F 2199/220 and L/L 2251/2252 contribute to binding membranes of physiologically relevant PS content. This is the first experimental data validating the hydrophobic membrane-binding motif identified in the crystal structure.

ACCESSION NUMBER: 2001:322378 BIOSIS
DOCUMENT NUMBER: PREV200100322378
TITLE: Four hydrophobic amino acids of the factor VIII C2 domain contribute to the membrane-binding motif.
AUTHOR(S): Gilbert, Gary E. [Reprint author]; Kaufman, Randall J.; Arena, Andrew A. [Reprint author]; Miao, Hongzhi; Pipe, Steven
CORPORATE SOURCE: Medicine, Harvard Medical School, Boston, MA, USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 633a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 5 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI **Factor VIII:c** concentrate virus inactivated:
Progress in purification by using classic chromatographic methods.
AB This study was carried out with the aim of developing a production process for the manufacture of a highly purified factor VIII concentrate which is virus inactivated by pasteurization in liquid phase. Beside standard plasma protein separation techniques, the procedure uses a chromatographic step on anion exchanger, whose selectivity is increased by using high, but not destabilizing **salt** concentrations. The final product before stabilization has a specific activity higher than 300 IU/mg of protein, namely the highest specific activity reported for human factor VIII concentrates purified without the use of immunoabsorbents.

ACCESSION NUMBER: 1993:182887 BIOSIS
DOCUMENT NUMBER: PREV199395093337

TITLE: **Factor VIII:c** concentrate virus inactivated: Progress in purification by using classic chromatographic methods.
AUTHOR(S): Arrighi, Silvana [Reprint author]; Pacenti, Lorenzo; Borri, Maria Giuseppina
CORPORATE SOURCE: Sclavo Biotechnol. Cent., Via Fiorentina 1, I-53100 Siena, Italy
SOURCE: Vox Sanguinis, (1993) Vol. 64, No. 1, pp. 13-18.
CODEN: VOSAAD. ISSN: 0042-9007.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Apr 1993
Last Updated on STN: 10 Apr 1993

L2 ANSWER 6 OF 16 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
TI THE ASSAY OF **FACTOR-VIII C** IN HEPARINIZED PLASMA A POLYBRENE NEUTRALIZATION METHOD.
AB Factor VIII coagulant activity (VIII:C) has been shown by several investigators to exhibit increased stability in vitro when physiological levels of palsma ionized calcium are maintained by anticoagulation with heparin rather than citrate. An increase in initial activity of VIII:C in heparin over that of VIII:C in citrate has been reported but this has not been confirmed. In order to assay VIII:C in heparinized plasma, the heparin anticoagulant effect must be excluded without interfering with the validity of the assay. A one-stage clotting assay for VIII:C has been developed where heprin is neutrlized by Polybrene, a synthetic polymerized quaternary ammonium **salt**. VIII:C may be accurately measured by this method which satisfies the requirements for a valid assay of parallelism and linearity.
ACCESSION NUMBER: 1986:297037 BIOSIS
DOCUMENT NUMBER: PREV198682030943; BA82:30943
TITLE: THE ASSAY OF **FACTOR-VIII C** IN HEPARINIZED PLASMA A POLYBRENE NEUTRALIZATION METHOD.
AUTHOR(S): CUMMING A M [Reprint author]; WENSLEY R T; DELAMORE I W
CORPORATE SOURCE: UNIV, DEP CLIN HAEMATOL, ROYAL INFIRMARY, OXFORD RD, MANCHESTER M13 9WL, UK
SOURCE: Thrombosis and Haemostasis, (1986) Vol. 55, No. 1, pp. 58-60.
CODEN: THHADQ. ISSN: 0340-6245.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 Jul 1986
Last Updated on STN: 25 Jul 1986

L2 ANSWER 7 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI **Factor VIII:c** Concentrate virus inactivated: Progress in purification by using classic chromatographic methods.
AB This study was carried out with the aim of developing a production process for the manufacture of a highly purified factor VIII concentrate which is virus inactivated by pasteurization in liquid phase. Beside standard plasma protein separation techniques, the procedure uses a chromatographic step on anion exchanger, whose selectivity is increased by using high, but not destabilizing **salt** concentrations. The final product before stabilization has a specific activity higher than 300 IU/mg of protein, namely the highest specific activity reported for human factor VIII concentrates purified without the use of immunoabsorbents.
ACCESSION NUMBER: 93047172 EMBASE
DOCUMENT NUMBER: 1993047172
TITLE: **Factor VIII:c** Concentrate virus inactivated: Progress in purification by using classic chromatographic methods.

AUTHOR: Arrighi S.; Pacenti L.; Borri M.G.
CORPORATE SOURCE: Sclavo Biotechnology Center, Via Florentina 1,I-53100 Siena, Italy
SOURCE: Vox Sanguinis, (1993) Vol. 64, No. 1, pp. 13-18. .
ISSN: 0042-9007 CODEN: VOSAAD
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 1993
Last Updated on STN: 7 Mar 1993

L2 ANSWER 8 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI The assay of **factor VIII:C** in heparinized plasma: A polybrene neutralization method.
AB Factor VIII coagulant activity (VIII:C) has been shown by several investigators to exhibit increased stability in vitro when physiological levels of plasma ionized calcium are maintained by anticoagulation with heparin rather than citrate. An increase in initial activity of VIII:C in heparin over that of VIII:C in citrate has been reported but this has not been confirmed. In order to assay VIII:C in heparinized plasma, the heparin anticoagulant effect must be excluded without interfering with the validity of the assay. A one-stage clotting assay for VIII:C has been developed where heparin is neutralized by Polybrene®, a synthetic polymerized quaternary ammonium **salt**. VIII:C may be accurately measured by this method which satisfies the requirements for a valid assay of parallelism and linearity.
ACCESSION NUMBER: 86151294 EMBASE
DOCUMENT NUMBER: 1986151294
TITLE: The assay of **factor VIII:C** in heparinized plasma: A polybrene neutralization method.
AUTHOR: Cumming A.M.; Wensley R.T.; Delamore I.W.
CORPORATE SOURCE: University Department of Clinical Haematology, Royal Infirmary, Manchester M13 9WL, United Kingdom
SOURCE: Thrombosis and Haemostasis, (1986) Vol. 55, No. 1, pp. 58-60. .
CODEN: THHADQ
COUNTRY: Germany
DOCUMENT TYPE: Journal
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

L2 ANSWER 9 OF 16 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
TI Isolation of human **factor VIII:C** by preparative high-performance size-exclusion chromatography.
AB Human Factor VIII procoagulant protein (VIII:C) is a plasma protein that participates in the cascade of events leading to blood coagulation. It is absent or defective in patients with hemophilia A. In vivo **Factor VIII:C** associates with Von Willibrand factor and its multimers to form a high-molecular-weight particle that can be dissociated into a lower-molecular-weight form in the presence of high concentrations of **salt**. We have been able to purify rapidly **Factor VIII:C** on a large scale by sequential high-performance size-exclusion chromatography (HPSEC) under conditions of first low **salt** and then high **salt** concentration. Reconstituted

commercial **Factor VIII:C** concentrate was purified by chromatography on a preparative HPSEC column (Toyo Soda, 60 x 2.5 cm, 300 ml) in 0.05 M imidazole buffer, (pH 7.0), containing 0.15 M sodium chloride. **Factor VIII:C** activity was eluted in the void volume in less than 20 min as a high-molecular-weight particle, well separated from low-molecular-weight contaminants. Purification was 20-fold, with a yield of 80%. Up to 4 g of Factor VIII concentrate could be purified at one time in this manner. This material was then concentrated and made 0.35 M in calcium chloride prior to re-chromatography on the same column in a buffer containing 0.30 M calcium chloride. Under these conditions, **Factor VIII:C** activity was eluted in the inner volume of the column at a position corresponding to a molecular weight of several hundred thousand in less than 1 h. It was well separated from both larger proteins and smaller peptide fragments. Analysis of the preparation with radiolabelled antibody to human **Factor VIII:C** antigen indicated that at least two molecular weight forms of **Factor VIII:C** were present.

ACCESSION NUMBER: 85169368 EMBASE
DOCUMENT NUMBER: 1985169368
TITLE: Isolation of human **factor VIII:C** by preparative high-performance size-exclusion chromatography.
AUTHOR: Herring S.W.; Shitanishi K.T.; Moody K.E.; Enns R.K.
CORPORATE SOURCE: Research Laboratories, Alpha Therapeutic Corporation, Los Angeles, CA 90032, United States
SOURCE: Journal of Chromatography, (1985) Vol. VOL. 326, pp. 217-224. .
CODEN: JOCRAM
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
025 Hematology
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

L2 ANSWER 10 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Use of purified prothrombin in producing pharmaceutical preparation comprising prothrombin as single active component, for treating factor VIII inhibitor conditions, hemophilia A or B, or von Willebrand disease.
AN 2004-662614 [65] WPIDS
AB AU2003204479 A UPAB: 20041011
NOVELTY - Use of purified prothrombin (I) in producing pharmaceutical preparation comprising prothrombin as single active component, for treating factor VIII inhibitor conditions, hemophilia A or B, or von Willebrand disease, is new.

DETAILED DESCRIPTION - Use of a purified prothrombin (I) in the producing a pharmaceutical preparation comprising prothrombin as single active component, for treating factor VIII inhibitor conditions, hemophilia A or B or von Willebrand disease, or for treating patients with impaired thrombin generation, caused by the absence or functional defect of one or several factors of the extrinsic or intrinsic coagulation other than Factor II, by the formation of antibodies to one or several of these factors or by lack of the cellular receptor for one or several of these factors.

ACTIVITY - Hemostatic.

The in vivo efficacy of prothrombin to treat factor VIII inhibitor conditions was tested as follows. White New Zealand rabbits (hemophilia rabbit model, 2 kg) were anesthetized. Then, right femoral vein was prepared and a permanent venous access was established. Through the latter, 0.5 ml/kg body weight of human factor VIII inhibitor plasma (1500 BU/ml) were infused during 10 minutes and 30 minutes after the end of

infusion, the bleeding characteristic was determined by using a modified method as described in Giles et al., Blood 60:727-730 (1982). To determine the bleeding characteristics, the fur surrounding the claw of the hind paw of the rabbit was shaved to prevent blood emerging at the later, and bleeding from being absorbed by the fur. The nail cuticle was injured by nail clipper. Blood was collected for 30 minutes, and then the wound was cauterized if the bleeding had not stopped. To quantitate the bleeding characteristic, the samples were extracted with 0.04% ammonium hydroxide solution for 5 hours, where the erythrocytes in the blood, were lysed. The hemoglobin was extracted and quantitated photometrically at 416 nm against a calibration curve, after 10 minutes sonication. The bleeding characteristics of the nail cutting were determined by graphically plotting the amounts of blood per 2 minutes fraction against time. The accumulated blood loss was determined by graphically plotting the volume of the individual blood fractions against time. The slope of the cumulative bleeding between 10 and 20 minutes was taken as a relevant bleeding criterion. The increase of the bleeding characteristic in 10-20 minutes observation intervals served as a measure for the intensity of bleeding. An increase equal zero meant that the bleeding had stopped, an increase greater than 0 with a correlation coefficient of greater than 0.8 meant that there was a constant bleeding. Under the test conditions, healthy rabbits had a bleeding intensity of less than 2 micro l blood/minute. Factor VIII inhibitor rabbits exhibited a bleeding intensity of 50 micro l blood/minute.

MECHANISM OF ACTION - Inhibitor of thrombin.

USE - (I) is useful for treating factor VIII inhibitor conditions, hemophilia A or B, or von Willebrand disease which involves administering a pharmaceutical preparation comprising (I) as single active component and a carrier, to a patient in need of the treatment, and for treating patients with impaired thrombin generation, caused by the absence or functional defect of one or several factors of the extrinsic or intrinsic coagulation other than Factor II, by the formation of antibodies to one or several of these factors or by lack of the cellular receptor for one or several of these factors (claimed).

(I) is useful for treating blood coagulation disorders.

ADVANTAGE - (I) can be produced by recombinant techniques (claimed), provides safe and simple method of treating blood coagulation disorders, within short time. (I) is highly pure.

Dwg.0/0

ACCESSION NUMBER: 2004-662614 [65] WPIDS
DOC. NO. NON-CPI: N2004-524620
DOC. NO. CPI: C2004-236697
TITLE: Use of purified prothrombin in producing pharmaceutical preparation comprising prothrombin as single active component, for treating factor VIII inhibitor conditions, hemophilia A or B, or von Willebrand disease.
DERWENT CLASS: B04 D16 P31
INVENTOR(S): EIBL, J; SCHWARZ, H; TURECEK, P
PATENT ASSIGNEE(S): (IMMO) IMMUNO AG
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
AU 2003204479	A1	20030626	(200465)*		78

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
AU 2003204479	A1 Div ex	AU 2000-71586	20001115
		AU 2003-204479	20030602

PRIORITY APPLN. INFO: AU 2000-71586 20001115; AU
2003-204479 20030602

L2 ANSWER 11 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI New stabilised Factor VIII solns. with high specific activity - contain aminoacid and opt. detergent or organic polymer.
AN 1992-341536 [42] WPIDS
AB EP 508194 A UPAB: 19931115
Stabilised Factor VIIIC solns. (A) containing an aminoacid or **salt** or derivative and opt. a detergent or organic polymer are new. Medicaments (B) prepared from (A) are also claimed.
The amioacid can have the L- and/or D-configuration and is pref. a natural, especially basic, aminoacid, partic. arginien (opt. in combination with glycine), lysine or ornithine. Derivs. are, e.g., those having an amino and/or guanidino gp., e.g., guanidinoacetic acid. The concentration of aminoacid is pref. 0.001-1 mol/l.
Detergents are, e.g., Tween (RTM) 20 and 80 and the polymer is, e.g., polyethylene glycol 1500.
USE/ADVANTAGE - (B), which contain Factor VIIIC isolated from human serum or prepared by recombinant DN techonology, are used for the treatment of haemophilia. In contrast to known prepns. stabilised with albumin, (A) contain no foreign proteins which could cause immunlogical problems and have specific activities of at least 200 IU/ml and above 2000 IU/mg.
Dwg.0/0
ABEQ US 5565427 A UPAB: 19961124
A stabilised solution with **factor VIII:C** activity containing **factor VIII:C**, an amino acid or one of its salts or homologues and a detergent or an organic polymer, wherein the specific **factor VIII:C** activity is at least 1000 IU/mg, is new.
Dwg.0/0
ABEQ EP 508194 B UPAB: 19980119
Stabilised Factor VIIIC solns. (A) contg. an aminoacid or **salt** or deriv. and opt. a detergent or organic polymer are new. Medicaments (B) prepd. from (A) are also claimed.
The amioacid can have the L- and/or D-configuration and is pref. a natural, esp. basic, aminoacid, partic. arginien (opt. in combination with glycine), lysine or ornithine. Derivs. are, e.g., those having an amino and/or guanidino gp., e.g., guanidinoacetic acid. The concn. of aminoacid is pref. 0.001-1 mol/l.
Detergents are, e.g., Tween (RTM) 20 and 80 and the polymer is, e.g., polyethylene glycol 1500.
USE/ADVANTAGE - (B), which contain Factor VIIIC isolated from human serum or prepd. by recombinant DN techonology, are used for the treatment of haemophilia. In contrast to known prepns. stabilised with albumin, (A) contain no foreign proteins which could cause immunlogical problems and have specific activities of at least 200 IU/ml and above 2000 IU/mg.
Dwg.0/0
ACCESSION NUMBER: 1992-341536 [42] WPIDS
DOC. NO. CPI: C1992-151821
TITLE: New stabilised Factor VIII solns. with high specific activity - contain aminoacid and opt. detergent or organic polymer.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): FREUDENBERG, W
PATENT ASSIGNEE(S): (BEHW) BEHRINGWERKE AG; (CENT-N) CENTEON PHARMA GMBH; (AVET) AVENTIS BEHRING GMBH
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 508194	A1	19921014	(199242)*	GE	5
R: AT BE CH DE DK ES FR GB GR IT LI LU NL PT SE					
DE 4111393	A	19921015	(199243)		5
AU 9214702	A	19921015	(199249)		
CA 2065553	A	19921010	(199252)		
JP 05097702	A	19930420	(199320)		4
AU 651188	B	19940714	(199432)		
US 5565427	A	19961015	(199647)		3
EP 508194	B1	19971210	(199803)	GE	6
R: AT BE CH DE DK ES FR GB GR IT LI LU NL PT SE					
DE 59209051	G	19980122	(199809)		
ES 2111579	T3	19980316	(199817)		
KR 231398	B1	19991115	(200111)		
IE 82191	B	20020403	(200235)		
JP 2002097199	A	20020402	(200238)		4
US 5565427	C1	20020723	(200259)		
CA 2065553	C	20030610	(200345)	EN	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 508194	A1		EP 1992-104944	19920321
DE 4111393	A		DE 1991-4111393	19910409
AU 9214702	A		AU 1992-14702	19920408
CA 2065553	A		CA 1992-2065553	19920408
JP 05097702	A		JP 1992-85806	19920408
AU 651188	B		AU 1992-14702	19920408
US 5565427	A	Cont of	US 1992-864610	19920407
		Cont of	US 1993-82911	19930629
			US 1994-235241	19940429
EP 508194	B1		EP 1992-104944	19920321
DE 59209051	G		DE 1992-509051	19920321
			EP 1992-104944	19920321
ES 2111579	T3		EP 1992-104944	19920321
KR 231398	B1		KR 1992-5733	19920407
IE 82191	B		IE 1992-1124	19920408
JP 2002097199	A	Div ex	JP 1992-85806	19920408
			JP 2001-220843	19920408
US 5565427	C1	Cont of	US 1992-864610	19920407
		Cont of	US 1993-82911	19930629
			US 1994-235241	19940429
CA 2065553	C		CA 1992-2065553	19920408

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 651188	B	Previous Publ.	AU 9214702
DE 59209051	G	Based on	EP 508194
ES 2111579	T3	Based on	EP 508194

PRIORITY APPLN. INFO: DE 1991-4111393 19910409

L2 ANSWER 12 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Factor VIII complex purificn. by heparin affinity chromatography - involves eluting with aqueous calcium chloride solution to recover intact complex with high specific activity.
AN 1991-038699 [06] WPIDS
AB EP 411810 A UPAB: 19930928

Process for Factor VIII complex from an impure protein fraction containing it comprises affinity chromatography on a heparin coupled chromatographic medium, elution with aqueous CaCl2, and recovery of Factor VIII complex from the eluate.

Factor VIII complex from cryoppte is pref. subjected to usual preliminary purificn. and virus inactivation steps. The chromatographic medium is pref. activated aldehyde-agarose resin (Actigel-A; RTM), coupled with heparin in e.g. 0.1M phosphate buffer, pH 6.5-7.5, containing 0.1M NaCNBH3, for 12-20 hrs at 4-30 deg.C. Amount of heparin is pref. 250-2000, especially ca. 1000 units/ml.gel. About 20 units **Factor VIII :C** activity are applied/ml heparin coupled medium, and extraneous proteins are removed by washing with e.g. 5-10 vols. of 0.01-0.05M buffer (e.g. imidazole buffer), pH6.5-7.5, containing 0.1-0.15M of a **salt**, e.g. LiCl, KCl, NaCl. Pref. the washing buffer is 0.02M imidazole byufbuffer, pH6.8, contg.0.15M NaCl.

USE/ADVANTAGE - Used for recovery of high specific activity Factor VIII complex from blood plasma-derived fractions, from recombinant DNA prods., or especially from Intact complex is isolated so there is no need to add extraneous proteins to stabilise the **Factor VIII: C** activity. The prod. can have a final specific activity of 30-60 units/mg, c.f. 5-10 units/mg for known methods where **Factor VIII:C** is dissociated from the complex. Batch or column methods may be used.

0/0

ABEQ US 5110907 A UPAB: 19930928

Sepn. and purificn. of Factor VIII complex from impure aq. soln. (cryoppt.) comprises absorption on a heparin-modified chromatographic media to bind the Factor VIII complex to heparin, followed by elution from CaCl2-contg. aq. soln.

Pref. the CaCl2 is 0.01-0.3(0.05-0.2)(0.1)M at pH 6.5-7.5(6.8) with 0.01-0.05(0.02) M imidazole buffer.

USE - Factor VIII is used to induce blood coagulation in treatment of haemophilia, etc.

ABEQ EP 411810 B UPAB: 19951211

A process for separating Factor VIII complex from an impure protein fraction containing Factor VIII complex, comprising providing an aqueous solution of the impure protein fraction containing Factor VIII complex, applying the impure protein fraction solution to a heparin coupled chromagraphic medium to bind Factor VIII complex to the heparin ligand of the chromatographic medium, characterised in that: the Factor VIII complex is eluted from the chromatographic medium using an aqueous solution containing CaCl2 as the eluting agent, and recovering Factor VIII complex from the eluate.

Dwg.0/0

ACCESSION NUMBER: 1991-038699 [06] WPIDS
DOC. NO. CPI: C1991-016567
TITLE: Factor VIII complex purificn. by heparin affinity chromatography - involves eluting with aqueous calcium chloride solution to recover intact complex with high specific activity.
DERWENT CLASS: B04
INVENTOR(S): BHATTACHAR, P; KOSOW, D P; STERNBURG, C F; BHATTACHARYA, P
PATENT ASSIGNEE(S): (ALPH-N) ALPHA THERAPEUTIC CORP
COUNTRY COUNT: 5
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 411810	A	19910206	(199106)*		
R: DE ES GB SE					
US 5110907	A	19920505	(199221)		9
EP 411810	B1	19951108	(199549)	EN	13

R: DE ES GB SE
DE 69023413 E 19951214 (199604)
ES 2078947 T3 19960101 (199608)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 411810	A	EP 1990-308104	19900724
US 5110907	A	US 1989-388254	19890801
EP 411810	B1	EP 1990-308104	19900724
DE 69023413	E	DE 1990-623413	19900724
		EP 1990-308104	19900724
ES 2078947	T3	EP 1990-308104	19900724

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 69023413	E Based on	EP 411810
ES 2078947	T3 Based on	EP 411810

PRIORITY APPLN. INFO: US 1989-388254 19890801

L2 ANSWER 13 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI **Factor VIII c** protein purificn. for e.g. haemophilia treatment - by adsorption onto solid support carrying phospholipid(s) and eluting with **salt** solution.
AN 1989-032186 [04] WPIDS
AB US 4795806 A UPAB: 19930923
Hioh purity protein (I) with **Factor VIII:C** procoagulent activity is prepared by: (1) Adsorbing Fator VIII:C onto a rigid support coupled to one or more of phosphatidyl serine, phosphatidyl choline, or phosphatidyl ethanolamine; the total of the latter two being 10-20 weight% of the phospholipids present. (2) Eluting (I) from the support with a **salt** solution which is neither denaturing nor reduces the procoagulent activity of (I).

The concentrated (I) can be obtd. from plasma obtd. from humans, bovines or porcines or can be obtd. from a genetically lugweered source. The **salt** may be NaCl, CaCL2, LiCl or KCl.

USE - Treatment of bleeding disorders, such as haemophilia. The method has the advantage over the use of columns carrying the appropriate mono-clonal antibody, that the potentially antigenic uncloned antibodies do not contaminate the prod. by leaching from the column. The relatively high cost of preparing monoclonal antibodies is avoided.

0/0

ABEQ EP 303064 B UPAB: 19930923
A method for preparing high purity protein having **Factor VIII:C** procoagulant activity or fusion products thereof, comprising the steps of: (a) adsorbing **Factor VIII:C** or fusion products thereof onto a rigid support to which has been coupled phospholipids selected from the group consisting of phosphatidylserine (PS) and phosphatidylserine in mixture with phosphatidylcholine (PS/PC) or phosphatidylethanolamine (PS/PE), said phosphatidylethanolamine or phosphatidylcholine when present being in an amount between 10% and 20% of said phospholipid, and (b) eluting the adsorbed **Factor VIII:C** or fusion products thereof with a non-denaturing **salt** solution, said **salt** solution being of a sufficient concentration to elute **Factor VIII:C** or fusion products thereof while maintaining the activity of **Factor VIII:C**.

0/0

ACCESSION NUMBER: 1989-032186 [04] WPIDS
DOC. NO. CPI: C1989-014024
TITLE: **Factor VIII c** protein purificn. for e.g. haemophilia treatment - by adsorption onto solid support carrying phospholipid(s) and eluting with **salt** solution.
DERWENT CLASS: B04 D16
INVENTOR(S): BROWN, J E; COWGILL, C A
PATENT ASSIGNEE(S): (MILE) MILES INC; (MILE) MILES LAB INC
COUNTRY COUNT: 14
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4795806	A	19890103	(198904)*		6
EP 303064	A	19890215	(198907)	EN	
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
EP 303064	B1	19930331	(199313)	EN	11
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 3879803	G	19930506	(199319)		
ES 2053631	T3	19940801	(199432)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4795806	A	US 1987-74123	19870716
EP 303064	A	EP 1987-111301	19870716
EP 303064	B1	EP 1988-111301	19880714
DE 3879803	G	DE 1988-3879803	19880714
		EP 1988-111301	19880714
ES 2053631	T3	EP 1988-111301	19880714

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3879803	G	Based on	EP 303064
ES 2053631	T3	Based on	EP 303064

PRIORITY APPLN. INFO: US 1987-74123 19870716

L2 ANSWER 14 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Ultra-purification process for polypeptide - by contact with an immobilised antibody, elution, passing through an affinity region and elution.
AN 1988-287485 [41] WPIDS
AB EP 286323 A UPAB: 19930923
Purificn. of a polypeptide from a mixture of polypeptides and other constituents comprises (a) immobilising an antibody which binds to the specific polypeptide to be purified, to a matrix before or after the polypeptide is added to the antibody, thereby immobilising the polypeptide in an immunoaffinity matrix, (b) eluting the polypeptide from the immobilised antibody by treating the polypeptide:immunoaffinity matrix with a desorbing substance, (c) passing the polypeptide to be purified through an affinity region capable of binding to the polypeptide and allowing contaminants to pass through and (d) eluting the purified polypeptide from the affinity region.

The affinity region may comprise an ion exchange matrix, e.g. an amino diethylaminoethyl or quaternary aminoethyl functional gp. deposited on a cellulosic matrix in a cartridge, or a hydrophobic interaction matrix containing e.g. phenyl or octyl functional gps. A virus-inactivating stage using an organic solvent and/or a detergent may be used. The organic

solvent is e.g. tri-n-alkyl phosphate, dialkyl ether or amyl acetate and suitable detergents are oxyethylated alkylphenols, sodium cholate and sodium deoxycholate.

USE/ADVANTAGE - The method can be used for purifying e.g. urokinase, streptokinase, fibrolase, Factor II, Factor V, Factor VII, Factor VIII, Factor IX, Factor X, Factor XI, Factor XII, Protein C and Protein S. The polypeptides can be isolated from e.g. blood plasma or tissue culture media and obtd. free of contaminants.

0/0

ABEQ EP 286323 B UPAB: 19940203

A method for purifying Factor VII:C from a mixture of polypeptides ad other constitutents comprising: (a) immobulising an antibody, which antibody binds by hydrophobic attraction to the Factor VII:C to be purified, to a matrix before or after said Factor VII:C is added to said antibody, thereby immobilising said **Factor VIII**:
C in an immunoaffinity matrix; (b) eluting the **Factor VIII:C** from the immobilised antibody by treating the **Factor VIII:C** immunoaffinity matrix with a desorbing substance to desorb the **Factor VIII**:
C from said matrix, thereby forming a **Factor VIII:C** desorbing substance mixture; (c) passing the **Factor VIII:C** to be purified through a second region capable of binding to the **Factor VIII:C** through a hydrophilic attraction, thereby binding the **Factor VIII:C** to the second region while allowing contaminants to pass through the seond region; (d) wherein the **Factor VIII:C** desorbing substance mixture is passed from the matrix of step (b) to the region of step (c) without further modification of the said mixture; and (e) eluting the purified **Factor VIII:C** from the said region.

Dwg.0/0

ABEQ US 5470954 A UPAB: 19960115

A method of purifying **Factor VIII:C** from a mixture of polypeptides and contaminants comprises:

(a) adsorbing an antibody to a matrix to form an immunoaffinity matrix, which antibody binds by hydrophobic attraction to the **Factor VIII:C** to be purified to form hydrophobic bonds, adding the mixture to said antibody before or after said antibody is bound to the matrix, thereby adsorbing said **Factor VIII:C** in the immunoaffinity matrix;

(b) eluting the **Factor VIII:C** from the immobilized antibody by treating the **Factor VIII**:
C:immunoaffinity matrix with a desorbing substance which breaks the hydrophobic bonds between the **Factor VIII**:
C and the immobilized antibody to desorb the **Factor VIII:C** from said matrix wherein the desorbing substance is a non-polar agent in a buffered **salt** solution;

(c) passing the **Factor VIII:C** to be purified through an affinity region which is an ion-exchange region capable of binding to the **Factor VIII:C**, thereby binding the **Factor VIII:C** to the affinity material while allowing the contaminants to pass through the affinity region; and

(d) eluting the purified **Factor VIII:C** from the affinity region.

Dwg.0/0

ACCESSION NUMBER: 1988-287485 [41] WPIDS
DOC. NO. CPI: C1988-127567
TITLE: Ultra-purification process for polypeptide - by contact with an immobilised antibody, elution, passing through an affinity region and elution.
DERWENT CLASS: B04
INVENTOR(S): GRIFFITH, M J; LIU, S; NESLUND, G; LIU, S L; NESLUND, G G

PATENT ASSIGNEE(S): (BAXT) BAXTER TRAVENOL LAB INC; (BAXT) BAXTER INT INC
COUNTRY COUNT: 15
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 286323	A	19881012	(198841)*	EN	17
R: AT BE CH DE ES FR GB IT LI NL SE					
DK 8801840	A	19881001	(198851)		
JP 01013099	A	19890117	(198908)		
EP 286323	B1	19931215	(199350)	EN	21
R: AT BE CH DE ES FR GB IT LI NL SE					
DE 3886249	G	19940127	(199405)		
ES 2061642	T3	19941216	(199505)		
US 5470954	A	19951128	(199602)		12
JP 2686766	B2	19971208	(199803)		13
CA 1339946	C	19980707	(199838)		
US 5470954	C1	20010206	(200112)		
DK 174968	B	20040405	(200425)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 286323	A		EP 1988-302905	19880331
JP 01013099	A		JP 1988-81160	19880331
EP 286323	B1		EP 1988-302905	19880331
DE 3886249	G		DE 1988-3886249	19880331
			EP 1988-302905	19880331
ES 2061642	T3		EP 1988-302905	19880331
US 5470954	A	CIP of	US 1987-32800	19870331
		Cont of	US 1988-167902	19880328
		Cont of	US 1992-887387	19920521
			US 1993-140695	19931021
JP 2686766	B2		JP 1988-81160	19880331
CA 1339946	C		CA 1988-562932	19880330
US 5470954	C1	CIP of	US 1987-32800	19870331
		Cont of	US 1988-167902	19880328
		Cont of	US 1992-887387	19920521
			US 1993-140695	19931021
DK 174968	B		DK 1988-1840	19880405

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3886249	G	Based on	EP 286323
ES 2061642	T3	Based on	EP 286323
JP 2686766	B2	Previous Publ.	JP 01013099
DK 174968	B	Previous Publ.	DK 8801840

PRIORITY APPLN. INFO: US 1988-167902 19880328; US
1987-32800 19870331; US
1992-887387 19920521; US
1993-140695 19931021

L2 ANSWER 15 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Purifying factor 8 c from plasma fractions - by adsorbing on hydrophobic matrix, washing to remove foreign proteins, then elution with surfactant containing buffer.
AN 1987-015785 [03] WPIDS
AB EP 209041 A UPAB: 19930922
Factor VIII:C (I) is purified from a source

also containing factor VIII:R (II) and other plasma proteins by (1) adjusting an aqueous solution of the starting materials to pH 6-8; (2) adding neutral **salt** to 0.1-2 M; (c) adosbring (I), (II) and other proteins onto a hydrophobic interaction matrix; (d) eluting (II) and foreign proteins by washing with aqueous solution (pH 6-8) containing 0.1-0.5 M CaCl2 and 0.1-40 weight% ethylene glycol; (e) washing with a buffer (pH 6.5-7.2) containing 0.01-0.6M NaCl, 0.01-0.2M glycine, 0.001-0.02M CaCl2 and 0.001-0.02M histidine; and finally (f) eluting (I) with and aqueous soln.containing 0.1-1 weight% surfactant.

USE/ADVANTAGE - (I) is useful for treatment of haemophilia. This method provides very pure (I) of high specific activity in good yield. The recovered eluate contains 10-50 U/ml and can be used directly or sterilised and freeze-dried for storage.

ABEQ US 4758657 A UPAB: 19930922

Improved sepn. of **Factor VIII:C** from a source material contg. it plus Factor VIII:R and other plasma proteins, comprises (a) absorbing **Factor VIII:C**/VIII:R and foreign protein complex from a plasma or commercial source into particles a monoclonal antibody specific to Factor VIII:R; (b) eluting **Factor VIII:C**, residual Factor VIII:R and foreign proteins with a saline soln.; (c) adjusting soln. to pH6.0-8.0; and (d) adding CaCl2 to concn. 0.1-2M.

Factor VIII:C, Factor VIII:R and foreign proteins are adsorbed from soln. onto a hydrophobic interaction matrix comprising pentyl agarose, hexyl agarose, heptyl agarose, octyl agarose, or phenyl agarose. Elution comprises washing with an aq. soln. of pH 6.0-8.0 contg. 0.1-0.5M CaCle and 0.1-40% w/w ethylene glycol. Matrix is further washed with a buffer soln. of pH 6.5-7.2 contg. 0.01-0.6M NaCl, 0.01-0.2M glycine, 0.001-0.020M CaCl2, and 0.001-0.020M histidine. **Factor VIII:C** is eluted by washing with an aq. soln. of 0.1-1% w/w surface active agent (e.g. (oxy-1,2-ethanediyl)20 monododeconsate sorbiton, etc.).

USE - For therapeutic administration to patients having haemophilia.

ACCESSION NUMBER: 1987-015785 [03] WPIDS
DOC. NO. CPI: C1987-006450
TITLE: Purifying factor 8 c from plasma fractions - by adsorbing on hydrophobic matrix, washing to remove foreign proteins, then elution with surfactant containing buffer.
DERWENT CLASS: B04
INVENTOR(S): FARB, D L; LANDABURU, R H
PATENT ASSIGNEE(S): (ARMO) ARMOUR PHARM CO LTD
COUNTRY COUNT: 16
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 209041	A	19870121	(198703)*	EN	24
R: AT BE CH DE FR GB IT LI LU NL SE					
AU 8660015	A	19870115	(198708)		
JP 62019534	A	19870128	(198710)		
DK 8603320	A	19870112	(198714)		
US 4758657	A	19880719	(198831)		5
ES 2000030	A	19871001	(198911)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 209041	A	EP 1986-109270	19860707
JP 62019534	A	JP 1986-160976	19860710
US 4758657	A	US 1985-753822	19850711
ES 2000030	A	ES 1986-222	19860710

PRIORITY APPLN. INFO: US 1985-753822 19850711

L2 ANSWER 16 OF 16 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
TI Purificn. of protein especially of antihaemophilic factor-VII-C - comprises column chromatography in presence of hydration additive, especially sugar, poly hydric alcohol, aminoacid or **salt**.
AN 1986-225369 [34] WPIDS
AB WO 8604486 A UPAB: 19930922
Purificn. of a protein (I) by column chromatography comprises exposing the (I) to the presence, as hydration additive, of a sugar, polyhydric alcohol, amino acid or **salt** at a concentration sufficient to increase the recovery, purity or resolution of (I) recovered from the column.
USE/ADVANTAGE - (I) is especially antihaemophilic **factor VIII:C** (AHF) for use in correcting the clotting defect of haemophilic plasma. It is purified with high recovery and high resolution, and high purity prods. are obtd. The procedure is economic, especially for AHF prods., and (I) after purificn. have a lower concentration of contaminating viruses. (I) may also be a blood coagulant factor, albumin or immunoglobulin.
0/3
ABEQ US 4743680 A UPAB: 19930922
Protein having antihaemophilic factor activity is purified in an ion-exchange chromatography column, by (a) equilibrating the column; (b) loading a sample contg. the protein and adsorbing it to the column; (c) washing the column; (d) eluting adsorbed protein from column by causing it to desorb; and (e) recovering purified prod.
Process comprises adding to the column a hydration additive in amt. to selectively increase electrostatic forces on the surface of the protein and concomitantly decrease its hydrophobicity to promote adsorption of protein on the column. Hydration additive comprises sugar or polyhydric alcohol added during stage (a), (b) and/or (c).
ADVANTAGE - Has lower concn. of contaminating proteins.
ABEQ US 4847362 A UPAB: 19930922
Protein, having antihemophilic factor (AFH) activity is purified by column chromatography in a column (I) behaving predominantly as a hydrophobic affinity chromatography column. Firstly, (I) is equilibrated. Then a sample contg. the protein is loaded on (I), causing the protein to adsorb on (I). (I) is then washed. The adsorbed protein is eluted from (I) by causing it to desorb from (I). Finally, the protein is recovered in purified form. The improvement comprises adding to (I) a cpd. comprising an effective amt. for selectively increasing the electrostatic forces on the surface of the protein, and concommitantly decreasing the hydrophobicity of the protein, of a hydration additive (II) selected from sugars and polyhydric alcohols. (II) is added during the elution of adsorbed protein from (I), thereby promoting the desorption of the protein from (I).
ADVANTAGE - Method is provided for purifying AFH and other proteins, from biological fluids, in high yield over the starting material.
ABEQ US 4952675 A UPAB: 19930922
Protein having antihaemophilic factor activity is purified by chromatography in a column behaving mainly as a hydrophobic affinity chromatography column.
Process comprises (a) equilibrating the column; (b) loading a protein-contg. sample onto column to adsorb it; (c) washing column; (d) eluting adsorbed protein by causing its desorption; and (e) recovering purified protein. Substance which selectively increases the electrostatic forces on the protein surface is added to the column, which also decreases its hydrophobicity.
ADVANTAGE - High yield is obtd. at lower cost with lower concn. of contaminating viruses.

ACCESSION NUMBER: 1986-225369 [34] WPIDS
DOC. NO. CPI: C1986-097252
TITLE: Purificn. of protein especially of antihaemophilic factor-VII-C

- comprises column chromatography in presence of hydration additive, especially sugar, poly hydric alcohol, aminoacid or **salt**.

DERWENT CLASS: A96 B04
INVENTOR(S): JOHNSON, A J; MATHEWS, R W
PATENT ASSIGNEE(S): (UYNY) UNIV NEW YORK STATE
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8604486	A	19860814	(198634)*	EN	40
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU BR DK FI JP KR NO					
AU 8654540	A	19860826	(198646)		
NO 8603902	A	19861215	(198705)		
EP 211895	A	19870304	(198709)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
ES 8702432	A	19870316	(198716)		
BR 8605129	A	19870505	(198724)		
FI 8603954	A	19860930	(198727)		
JP 62501562	W	19870625	(198731)		
DK 8604486	A	19861128	(198745)		
US 4743680	A	19880510	(198821)		
CN 86102829	A	19871104	(198846)		
US 4847362	A	19890711	(198935)		
US 4952675	A	19900828	(199037)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8604486	A	WO 1986-US228	19860131
EP 211895	A	EP 1986-901251	19860131
ES 8702432	A	ES 1986-551483	19860131
JP 62501562	W	JP 1986-501112	19860131
US 4743680	A	US 1985-697267	19850201
US 4847362	A	US 1987-122372	19871119
US 4952675	A	US 1988-291516	19881229

PRIORITY APPLN. INFO: US 1985-697267 19850201; US 1987-122372 19871119

Refine Search

Search Results -

Terms	Documents
6465624.pn.	1

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L19

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Monday, May 08, 2006 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L19	6465624.pn.	1	L19
L18	6414125.pn.	1	L18
L17	6831159.pn.	1	L17
DB=PGPB; PLUR=YES; OP=OR			
L16	6831159.pn.	0	L16
L15	L14 and l11	0	L15
L14	l12 and (Factor VIII:C)	513	L14
L13	L12 and l11	0	L13
L12	fischer.in.	1886	L12
L11	L10 and (high molecular weight multimer)	165	L11
L10	L8 and ("200-300")	165	L10
L9	L8 and (greater than 200mM)	7626	L9
L8	L7 and (salt concentration)	8830	L8
L7	L6 and (step-wise elution)	8877	L7
L6	L5 and (cation exchanger)	31491	L6
L5	L4 and (free of platelet agglutinating vWF activity)	193903	L5
L4	(factor VIII:C)	321434	L4
L3	L1 and (substantially free)	1	L3
L2	L1 and (substantially free)	1	L2

L1	20050239171	1	L1

END OF SEARCH HISTORY